IN THE UNITED STATES PCT RECEIVING OFFICE

Applicant(s):	Gideon Schreiber	Docket No:	05558.0018.PCUS00
App. No.:	10/500,521	Art Unit:	1633
Conf. No.:	7709	Examiner:	Sajjadi, Fereydoun Ghotb
Int. Filing Date:	June 28, 2005	Title:	IFNAR2 MUTANTS, THEIR PRODUCTION AND USE

AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

Dear Sir:

In response to the Office Action mailed November 21, 2005 (the "Office Action"), and in accordance with the Rule of Practice, please enter the following amendments and consider the remarks below. Submitted herewith is a Petition for a one-month Extension of Time together with the requisite fee of $120, which extends the deadline for filing the reply to March 21, 2006. No other fees are believed to be due, however, should any additional fees be deemed necessary in connection with the filing of this document, the Commissioner is hereby authorized to deduct any such fees from Deposit Account No. 08-3038 referencing the above-identified docket number.

I. Amendments To The Claims

1. - 61. (canceled)

62. (currently amended) An isolated IFNAR2 polypeptide, wherein said polypeptide is mutated at amino acid residues histidine 78 and asparagine 100 of the extracellular domain, and wherein said mutation synergistically increase the affinity for IFN-β compared to the wild type polypeptide, and wherein said polypeptide ~~has at least 70% identity to the wild type polypeptide~~is characterized by the following:

(a) histidine 78 is substituted by alanine; and

(b) asparagine 100 is substituted by alanine, aspartic acid or histidine.

63. (currently amended) The polypeptide of claim 62, wherein asparagine 100~~histidine 78~~ is substituted by aspartic acid~~alanine~~.

64. (currently amended) The polypeptide of claim 62, wherein asparagine 100 is substituted by ~~alanine, aspartic acid or~~ histidine.

65. (currently amended) The polypeptide of claim 62, wherein ~~both histidine 78 and~~ asparagine 100 ~~are~~ is substituted by alanine.

66. (previously presented) The polypeptide of claim 62, wherein the polypeptide comprises a sequence selected from the group consisting of SEQ ID NOS: 2, 3 and 4.

67. (previously presented) The polypeptide of claim 62, wherein the affinity to IFN-β is at least 30 pM.

68. (previously presented) The polypeptide of claim 62, wherein the affinity to IFN-β is at least 25 to 100-fold higher than the affinity of the wild type polypeptide.

69. (previously presented) The polypeptide of claim 62, wherein the polypeptide comprises the extracellular domain.

70. (previously presented) The polypeptide of claim 62, wherein the polypeptide is covalently bound to IFN.

71. (previously presented) The polypeptide of claim 70, wherein the IFN is IFN-β.

72. - 74. (canceled)

75. (currently amended) The polypeptide according to any one of claims 62-7174, wherein the polypeptide is a ~~fragment, analog, functional derivative or~~ fusion protein of IFNAR2.

76. (previously presented) A DNA encoding the polypeptide of claim 62.

77. (previously presented) The DNA of claim 76, wherein the polypeptide comprises a signal peptide sequence.

78. (previously presented) The DNA of claim 77, wherein the signal peptide sequence is that of human growth hormone.

79. (previously presented) A vector comprising the DNA according to any one of claims 76-78, wherein the vector is capable of expressing the polypeptide in a prokaryotic host cell or eukaryotic host cell.

80. (previously presented) A host cell comprising the vector of claim 79.

81. (previously presented) A method of producing an IFNAR2 mutant polypeptide comprising:

(a) cultivating the cell of claim 80 under conditions that cause the expression of the polypeptide; and

(b) isolating the polypeptide.

82. (previously presented) A composition comprising the polypeptide of claim 62 and optionally an IFN antagonist.

83. (previously presented) A method of treating a condition associated with modulation of IFN comprising administering to a patient in need thereof a therapeutically effective amount of the composition of claim 82, wherein the condition is selected from the group consisting of cancer, autoimmune disease and viral disease.

84. (withdrawn) The method of claim 83, wherein the cancer is selected from the group consisting of hairy cell leukemia, Kaposi's sarcoma, multiple myeloma, chronic myelogenous leukemia, non-Hodgkins's lymphoma and melanoma

85. (previously presented) The method of claim 83, wherein the autoimmune disease is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, myasthenia gravis, diabetes, lupus and ulcerative colitis.

86. (withdrawn) The method of claim 83, wherein the viral disease is selected from the group consisting of chronic granulomatous disease, condyloma acuminatum, juvenile laryngeal papillomatosis, hepatitis A, hepatitis B and hepatitis C.

II. Remarks

A. Amendments to the Claims

Claims 62-86 are pending in the application. Claims 1-61 were previously canceled. Claims 84 and 86 were previously withdrawn from consideration by the Examiner. With this amendment, Applicant cancels claims 72-74 and amends claims 62-65 and 75. Upon entry of these amendments, claims 62-71 and 75-86 will be pending with claims 62-71, 75-83 and 85 under active consideration.

Claim 62 is amended to recite that the polypeptide is characterized by a H78A mutation and either an N100A, N100D or N100H mutation, support for which may be found at page 29, lines 14-17 of the application as originally filed. Claim 62 is also amended to recite that the polypeptide is "isolated," support for which may be found through the application as originally filed.

Claim 63 is amended to recite that the polypeptide is characterized by an N100D mutation, support for which may be found at page 29, lines 14-17 of the application as originally filed.

Claim 64 is amended to recite that the polypeptide is characterized by an N100H mutation, support for which may be found at page 29, lines 14-17 of the application as originally filed.

Claim 64 is amended to recite that the polypeptide is characterized by an N100A mutation, support for which may be found at page 29, lines 14-17 of the application as originally filed.

Claim 75 is amended to recite that the polypeptide may be a fusion protein, support for which may be found at page 6, line 10 of the application as originally filed.

In view of the application as originally filed providing support for each of the amendments made herein, Applicant respectfully submits that no new matter has been added.

B. Patentability Rejections

1. 35 U.S.C. §101

At page 2 of the Office Action, the Examiner rejects claims 62-65 and 67-74 under 35 U.S.C. §101 as directed to non-statutory subject matter on the grounds that the claimed polypeptide may be a product of nature. Applicant respectfully disagrees. While Applicant believes that the Examiner has misapplied the statutory subject matter requirement, the claims have been amended to recite "isolated" in order to advance prosecution of this application.

2. 35 U.S.C. §112 – Written Description

At page 3 of the Office Action, the Examiner rejects claims 62-65, 67-83 and 85 under 35 U.S.C. §112 as failing to comply with the written description requirement. In the interest of advancing prosecution of the instant applicant, Applicant has amended the claims to be directed to individual species explicitly described in the application as originally filed. Accordingly, Applicant respectfully requests that the rejection for lack of written description support be reconsidered and withdrawn.

3. 35 U.S.C. §112 – Enablement

a. Claims 62-65, 67-83 and 85

At page 3 of the Office Action, the Examiner rejects claims 62-65, 67-83 and 85 under 35 U.S.C. §112 for lack of enablement. In the interest of advancing prosecution of the instant applicant, Applicant has amended the claims to be directed to individual species explicitly described in the application as originally filed. Accordingly, Applicant respectfully requests that the rejection for lack of enablement be reconsidered and withdrawn.

b. Claims 83 and 85

At page 9 of the Office Action, the Examiner also rejects claims 83 and 85 under 35 U.S.C. §112 for lack of enablement. The Examiner alleges that the use of an effective amount of the claimed polypeptide for treating an autoimmune disease or multiple sclerosis is not enabled "absent a strong showing by Applicant." The Examiner rejects the claims 83 and 85 because "[t]he specification fails to provide a description of what constitutes a therapeutically effective amount of a composition comprising a therapeutic

effective amount of a composition comprising the IFNAR2 mutated polypeptide." Applicant respectfully disagrees. Selecting the appropriate effective amount of a composition for a particular patient is well within the skill of the ordinary artisan and may be determined without undue experimentation. Accordingly, Applicant respectfully requests that the rejection for lack of enablement be reconsidered and withdrawn.

4. 35 U.S.C. §103(a)

a. Claims 62-76

At page 11 of the Office Action, the Examiner rejects claims 62-76 under 35 U.S.C. §103(a) over Piehler et al. ("Piehler"). The Examiner alleges that the claims are obvious because Piehler (i) describes the effects of the mutations at positions His 78 and Asp 100; (ii) provides the motivation to simultaneously mutate His 78 and Asp 100; and (iii) provides a reasonable expectation. Applicant respectfully disagrees. Application respectfully submits that the Examiner has failed to consider the evidence of secondary considerations.

Secondary considerations, such as unexpected results, must be considered in every case in which they are present. *See MPEP* § 2141. As stated at page 29, lines 14-17 and shown in Table 4, each of the claimed double mutants H78A/N100A, H78A/N100D and H78A/N100H cause a synergistic effect on the affinity of the polypeptide to IFNb compared to single mutations at H78 and N100. Piehler fails to teach or suggest such a result. Accordingly, Applicant respectfully requests that the rejection for obviousness be reconsidered and withdrawn.

b. Claims 77-81

At page 11 of the Office Action, the Examiner also rejects claims 77-81 under 35 U.S.C. §103(a) over Piehler and Campbell et al. ("Campbell"). As discussed above, Piehler fails to teach or suggest the synergistic effect of the claimed double mutants H78A/N100A, H78A/N100D and H78A/N100H. Campbell does nothing to remedy the defect of Piehler. Accordingly, Applicant respectfully requests that the rejection for obviousness be reconsidered and withdrawn.

C. Conclusion

In view of the above amendments and remarks, Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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